REMARKS

I. Amendments

By this amendment, claims 3 and 12 has been cancelled and new claim 21 has been added.

This amendment adds no new matter to the specification. Support for this amendment is found in the specification and claims as filed.

No amendment of inventorship is necessitated by this amendment.

II. Discussion of the Obviousness-Type Double Patenting Rejection

Claim 12 has been provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-6 of U.S. Patent No. 6,299,904.

By this amendment, Applicants have cancelled claim 12, thereby rendering the rejection moot.

Therefore, Applicants respectfully request withdrawal of the obviousness-type double patenting rejection.

III. Discussion of the Previous Rejection under 35 U.S.C. Sec. 102(b) over Ohno *et al.*

The rejection of claims 1-7, 9 and 13-17 under 35 U.S.C. Sec. 102(b) as anticipated by Ohno *et al.* (U.S. Patent No. 5,958,453) had previously been rejected. Since this rejection has not been repeated, Applicants assume it may have been overcome by their last response. For the record, Applicants respectfully request that the Examiner state that the Sec. 102(b) rejection over Ohno *et al.* has been overcome.

IV. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) over Ohno *et al.*

Claims 1-7 and 13-20 have been rejected under 35 U.S.C. Sec. 103(a) as allegedly obvious over Ohno *et al.*, U.S. Patent No. 5,958,453. For three reasons, the cited reference does not teach or suggest the Applicants' invention as set forth in the pending claims. Each reason will be discussed in the following paragraphs. Applicants invite the Examiner to address each aspect of Applicants' reasons for patentability separately, should she choose to maintain the rejection.

Reason 1: Cited Art Teaches Away From the Invention

The '357 reference does not teach that L-HPC is a choice for a solid formulation which disintegrates quickly. In the '357 reference, comparative examples are presented, wherein formulations with and without L-HPC are evaluated in terms of dissolution time. In every instance, the formulations including L-HPC demonstrate significantly longer dissolution times.

Specifically, in Example 4, without L-HPC a dissolution time of 45 seconds is recorded, whereas with L-HPC a buccal dissolution time more than twice slower (105 seconds) is recorded. In Example 5, without L-HPC a dissolution time of 28 seconds is recorded, whereas with L-HPC a buccal dissolution time which is three times slower (85 seconds) is recorded.

No one skilled in the art would have been motivated to add L-HPC to a preparation to improve disintegrability in light of the experimental results presented. Therefore, the '357 reference teaches away from the present invention.

Despite these results, Applicants were able to actually create a formulation wherein L-HPC is added and dissolution time is favorably affected. How is this possible, given the '357 reference? The answer is found in the paragraphs under Reason 2.

Reason 2: Cited Art Does Not Teach the Present L-HPC Component

The '357 reference does not teach or suggest the presently specified L-HPC merely because an L-HPC is added to certain formulations. The experimental evidence of the '357 reference proves this point, as the results which the Applicants set forth in the present application could not have been achieved before because the L-HPC now recited was not available at the time of the '357 reference. Had it been available, desirable dissolution times could have readily been obtained by the authors of the '357 reference. They were not because the L-HPC component of the present formulation was not available.

Documents to prove that low-substituted hydroxypropylcellulose having 5% to less than 7% was not available at the time of the '357 reference were previously submitted on January 15, 2002. A catalogue for the appropriate time period from Shin-Etsu Corp. (the supplier of L-HPC) shows that the presently claimed L-HPC was not sold. Additionally, a Declaration from a Shin-Etsu employee states that L-HPC having the low hydroxypropylcellulose content presently claimed was unavailable. Further evidence is provided by an author of the '357 reference (Mr. Ohno) who states that the L-HPC used in the experiments of the reference had a hydroxypropylcellulose content no lower than 10%; and moreover that there would have been no motivation to use L-HPC to improve oral formulations given the poor results which he reported.

The Examiner has stated previously that all of this evidence is not convincing because no surprising results are obtained. According to the Examiner, since the '357 reference indicates that formulations can be made having buccal dissolution times of 0.1 –1 minute; and the reference shows formulations including L-HPC; that the Applicants' invention as set forth in the pending claims is obvious. However, the Examiner has merely gleaned a point or two from this reference and quickly arrived at an erroneous assumption. One skilled in the art would not have interpreted the reference in this way, but rather would have taken the reference as a whole, and learned from the presented examples that L-HPC could **NOT** be used to achieve even the broadest stated range of buccal dissolution times (up to a minute). So the Examiner's statement that no unexpected results were obtained is just plain wrong.

The Examiner has ignored the principle that the cited art should be considered in its entirety. It has been stated that "[i]t is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art" in *In re Wesslau*, 353 F.2d 238, 241. This

statement characterizes what the Examiner has done in this instance to stretch the '357 reference such that it covers the present invention. Not only do the Applicants assert that the Examiner's characterization of what the '357 reference teaches those skilled in the art is wrong; but also they've provided a Declaration from Mr. Ohno (one actually skilled in the art) which verifies their point.

The Examiner has stated that "Ohno's teachings are relied upon within the four walls patent, Ohno cannot be limited to his best mode as described in the examples." in defense of her position. Applicants clearly are not so arguing, but rather urge that use of L-HPC in Ohno's formulations is not only not a best mode, it isn't any mode at all, as use of an L-HPC component did not work for the purposes intended.

Put another way, the '357 reference does not enable what the Examiner believes it discloses; i.e. – that L-HPC can be put into a formulation to achieve buccal dissolution time of 0.1 – 1.0 minutes.

Reason 3: Applicants' Method Claims Have Not Been Addressed

In the present application, independent method claims 18, 19 and 20 are pending. In independent method claim 18, a method for making a solid preparation having no roughness and improved chalky taste is disclosed; in independent method claim 19, a method for improving a solid preparation is disclosed; while in independent method claim 20, a method for treating certain conditions is disclosed. The Examiner has not even addressed these claims specifically with respect to the cited reference.

Applicants do not believe any of their methods are taught or suggested by the cited reference. If the Examiner chooses to maintain the rejection, Applicants respectfully request that she indicate where in the cited reference the subject matter of claims 18-20 is suggested.

Therefore, Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection over Ohno *et al.*

V. Discussion of the Rejection under 35 U.S.C. Sec. 103(a) over Ohno *et al.* in view of Shimizu *et al.*

Claims 9-12 have been rejected under 35 U.S.C. Sec. 103 (a) as allegedly obvious over Ohno *et al.*, U.S. Patent No. 5,958,453 in view of Shimizu *et al.*, U.S. Patent No. 6,299,904.

The Applicants assert that the '904 reference is not properly citable art, due to Applicants' earlier priority. Applicants submitted a Certified Translation of the Priority Documents with their previous response. Moreover, Applicants note that the Office Action Summary dated October 2, 2001 acknowledges that a Certified Copy of the Priority Document was received. As Applicants have perfected their priority, they believe this rejection should be moot. Applicants particularly do not understand the Examiner's request that the translation of the JP 9-136724 be provided, as this is not their priority document. Applicants respectfully request that the Examiner carefully review this point, and specifically state why the rejection is being maintained in light of their priority, should she choose to continue to maintain the rejection.

Therefore Applicants respectfully request withdrawal of the 35 U.S.C. Sec. 103(a) rejection over Ohno *et al.* in view of Shimizu *et al.*

VI. Discussion of the Rejection under 35 U.S.C. §103(a) over Ohno *et al.* in view of Shashoua *et al.*

The rejection of claims 10-12 under 35 U.S.C. Sec. 103(a) as allegedly obvious over the Ohno *et al.*, U.S. Patent No. 5,958,453 in view of Shashoua *et al.*, U.S. Patent No. 5,795,909 has been maintained.

The Examiner has indicated that the '909 reference has been cited because it recites some active ingredients in an oral dosage form. Although some active agents and tablet formulation are briefly mentioned, Applicants assert that the '909 reference would not have been consulted by one skilled in the art seeking to create a rapidly disintegrable solid preparation.

This reference is directed to conjugates useful for treating cell proliferative disorders, wherein an active agent is combined with another chemical compound. Examples of test solutions are provided; and it is indicated that intravenous administration of the conjugates are

preferable in the reference. One preparing to create a novel tablet or solid formulation would not have chosen to review and incorporate the teachings from a reference disclosing IV solutions. So there is no reason to combine the '909 reference with the '357 reference.

The Examiner continues to either ignore, or possibly not understand, the entirety of the '909 reference, wherein active agents are conjugated to another compound and the conjugate is put into a solution. A solution for IV use does not to have a property of rapid disintegrability; as it is already dissolved. So Applicants assert that although the Examiner's reason for combining the two references appears logical to the Examiner on paper, those skilled in the art would not have seen or made any connection between the two references.

Therefore, Applicants continue to assert that the two references would not have been combined by those skilled in the art; and moreover that the Examiner here again has merely gleaned a word or two from a reference without considering the teaching as a whole prior to making a broad characterization of the reference.

Therefore, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. Sec. 103(a) over Ohno *et al.*, U.S. Patent No. 5,958,453 in view of Shashoua *et al.*, U.S. Patent No. 5,795,909.

VII. Discussion of New Claim 21

By this amendment, new claim 21, directed to a tablet, has been added. This amendment adds no new matter to the specification. Claim 3 has been cancelled in light of this new independent claim.

In the new independent claim, a tablet which has no roughness and which are improved in chalky taste is recited. These virtues are imparted by the use of the recited specified low-substituted hydroxypropylcellulose (L-HPC).

This specific type of L-HPC was not sold when the invention disclosed in the '357 reference was made, as Applicants have explained in their response and accompanying supporting documents dated January 15, 2002.

Moreover, the '357 reference does not suggest that use of the specified L-HPC can lead to tablets having the special and advantageous characteristics of not being rough and not tasting so chalky. That is so because the L-HPC's available at the time of the invention of the '357 reference could not achieve this result.

Applicants claim tablets having a special ingredient (a specific type of L-HPC) which leads to an advantageous result (no roughness, less chalky taste). The '357 reference does not teach or suggest the specified L-HPC and also does not teach or suggest the characteristic imparted, since the L-HPC's of that time could not impart that characteristic.

VIII. Conclusion

Reconsideration of the claims as amended in view of the arguments made above is solicited. Should the Examiner believe that a conference with Applicants' attorney would advance prosecution of this application, she is respectfully requested to call Applicants' attorney.

Respectfully submitted,

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